# IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
# BOARD OF PATENT APPEALS AND INTERFERENCES



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| Appellant: | M. Rigdon Lentz | | |
| Serial No.: | 09/083,307 | Art Unit: | 3762 |
| Filed: | May 22, 1998 | Examiner: | W. Noggle |

For: METHOD AND COMPOSITIONS FOR TREATMENT OF CANCERS

Board of Patent Appeals and Interferences
United States Patent and Trademark Office
Washington, D.C. 20231



## REPLY BRIEF

Dear Sirs:

This Brief is submitted in Reply to the Examiner's Answer mailed October 2, 2000. Under 37 C.F.R. §1.7, the two-month period for response is extended to Monday, December 4, 2000. Submitted herewith is a Request for Oral Hearing.

Appellant refers the Board to the Appeal Brief filed July 12, 2000 for a full explication of the issues. Appellant addresses only certain salient points below. Pending claims 1-23 are set forth in the Appendix.

The Commissioner is hereby authorized to charge any necessary fee, or credit any overpayment to account number 01-2507.

There are No Related Appeals or Inteferences

Confirming the Examiner's understanding, there are no related appeals or interferences that will directly affect or be affected by or have a bearing on the decision in the pending appeal.

The Invention

The invention is the discovery that one can use a filter to selectively remove molecules of less than 120,000 Daltons from the blood of a patient and induce remission of cancer or other type of chronic disease. This process, in combination with certain

adjuvant therapies, can induce remission, and maintain the patient in remission. [Page 2, line 27 to page 3, line 27.] The process allows the patient to retain his immunoglobulins, thus preserving the patient's ability to fight infection.

The Rejections

Claims 1-4, 8, 9, 16, 18-20 and 22 were rejected under 35 U.S.C. §103 over U.S. Patent No. 4,708,713 to Lentz. Lentz ('713) discloses using a filter to remove components less than 1,000,000 Daltons, or less than 200,000 Daltons, especially an immune complex between 200,000 Daltons and 1,000,000 Daltons. [*see* Col. 6, lines 34-46].

Claim 21 was rejected under 35 U.S.C. §103 over Lentz ('713) in view of U.S. Patent No. 5,523,096 to Okarma. Okarma describes removal of cytokines for treatment of septic shock and capillary leak syndrome [col. 5, lines 25-28].

Claim 7 was rejected under 35 U.S.C. §103 over Lentz ('713) in view of Chen, J. Neurol. Neuropathol., vol. 56, pp. 541-550 (1997). Chen teaches that soluble TNF-alpha receptors are 55,000 and 75,000 Daltons in size, and suppress a patient's ability to fight cancers. [abstract, page 549].

Claims 5, 6, 10-15, 17 and 23 were rejected over Lentz ('713) in view of U.S. Patent No. 5,861,483 to Wolpe. Wolpe discloses polypeptides which are inhibitors of stem cell proliferation. [col. 5, lines 15-42].

The Examiner's Answer

Pages 9-10 of the Examiner's Answer acknowledge that Lentz, U.S. Patent No. 4,708,713, discloses filters with the ability to remove components having molecular weights of less than 1,000,000 Daltons, but also teaches removal of components less than 200,000 Daltons. The Examiner then concludes that Lentz does suggest using a filter having a "lower molecular weight cut-off. . .". At Page 12 of the Examiner's Answer, he concludes that "a prima facie case [of obviousness] has been made and set forth in the previous actions and further explained in this Examiner's Answer."

Appellant disagrees, for the reasons set forth below.

An Incorrect Legal Standard has been applied – Under In re Soni, Appellant's Showing of Unexpected Results is sufficient to overcome the rejection under 35 U.S.C. §103 over Lentz ('713)

In In re Soni, 54 F.3d 746, 750, 34 U.S.P.Q.2d 1684 (Fed. Cir. 1995), the Court of Appeals for the Federal Circuit reversed rejections under 35 U.S.C. §103 of patent application claims directed to an organic polymer. The specification stated that the claimed compositions had significantly improved physical and electrical properties compared to compositions using polymers having a molecular weight below 150,000. The Court noted that: "One way for a patent applicant to rebut a *prima facie* case of obviousness is to make a showing of 'unexpected results', *i.e.*, show that the claimed invention exhibits some superior property that a person of ordinary skill in the art would have found surprising or unexpected." Soni, at p. 750. The specification demonstrated an increase in peel strength, and improved resistivity and recovery behavior. Soni, at pp. 746-7. The court stated that:

> Mere improvement in properties does not always suffice to show unexpected results. In our view, however, when an applicant demonstrates substantially improved results, as Soni did here, and states that the results were unexpected, this should suffice to establish unexpected results in the absence of evidence to the contrary.

Soni, at p. 751.

The present case is apposite. Appellant has demonstrated that, unexpectedly, an immune response can be induced against transformed, disease, or infected tissue by removing components with a molecular weight below 120,000. This particular range is not suggested or disclosed by the prior art. The prior art discloses any number of possibilities, and even suggests that the proper range for removal is between 200,000 and 1,000,000 Daltons (see Lentz, U.S. Patent No. 4,708,713; Col. 6, lines 34-46). Employment of the unexpected finding by Appellant permitted the patients treated in the Examples to retain their immunoglobulin molecules and thus, their ability to ward off infections. The prior art would have stripped these patients of their immunoglobulins.

As in In re Waymouth, 499 F.2d 1273, 182 U.S.P.Q. 290 (C.C.P.A. 1974) (reversing §103 rejection of claims for arc tube with halogen and mercury atoms in the specified ratio of 0.08 to 0.75), Appellant has demonstrated the necessary unexpected results, and:

> Those results follow from the selection of appellant's critical range, which is narrower than the extremely broad inherently disclosed range of [the prior art].

Under *In re* Antonie, if the parameter optimized is not recognized to be a result-effective variable by the prior art, a rejection under 35 U.S.C. §103 over Lentz ('713) should be reversed

In In re Antonie, 559 F.2d 618, 195 U.S.P.Q. 6 (C.C.P.A. 1977), the court reversed rejections under 35 U.S.C. §103 of claims directed to a wastewater treatment device with a ratio of tank volume to water contactor area of 0.12 gal./square foot. The court stated that: "In this case, the invention as a whole is the ratio value of 0.12 and its inherent and disclosed property." *Id.*, at p. 619. The Patent Office had cited a reference which disclosed the basic structure of the device claimed by the appellant, but was "silent regarding quantitative design parameters other than to give data on a single example." *Id.*, at p. 619. The court stated:

> The controlling question is simply whether the differences (namely the value of 0.12 and its property) between the prior art and appellant's invention as a whole would have been obvious. The answer is no. It is impossible to recognize, from the experiment taught by El-Naggar [the prior art], that "treatment capacity" is a function of "tank volume" or the tank volume-to-contactor area ratio. Recognition of this functionality is essential to the obviousness of conducting experiments to determine the value of the "tank volume" ratio which will maximize treatment capacity. . .The experiments suggested by El-Naggar do not reveal the property which applicant has discovered, and the PTO has provided us with no other basis for the obviousness of the necessary experiments.

In reversing the rejection, the court concluded that "where a parameter optimized was not recognized to be a result-effective variable" discovery of an optimum value of a variable in a known process is not obvious. *Id.*, at p. 620.

As set forth above, the prior art did not suggest or disclose that the molecular weight threshold of 120,000 would be critical to allowing a patient to retain immunoglobulins, and thus preserve his ability to fight infections. Discovery of this 'result-effective variable' is solely within the present application. Therefore, the instant rejections under 35 U.S.C. §103 should be withdrawn.

The Claims do not Stand or Fall Together – However, if the rejection over Lentz ('713) is withdrawn, all other rejections are mooted

As stated in the Appeal Brief, the claims of the instant application do not stand or fall together. However, if the if the rejection over Lentz ('713) is withdrawn, all other rejections are mooted.

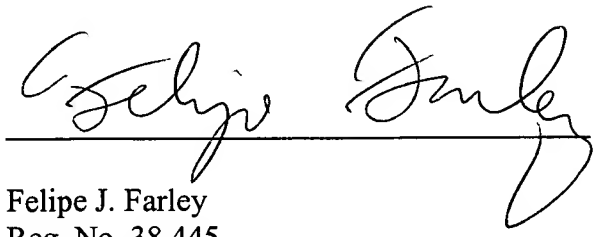
Summary

The Examiner has applied an incorrect legal standard. Appellant has demonstrated results of a different kind than the prior art: *i.e.*, permitting a patient to retain his immunoglobulins while inducing an immune response against transformed, diseased or infected tissue. Appellant recognized that only components of molecular weight less than 120,000 should be removed from the blood. The Examiner should accept these results as mandated by Soni. The case of Antonie also dictates that the Examiner acknowledge Appellant's discovery of this "result-effective variable", and withdraw the rejection under 35 U.S.C. §103.

Conclusion

For the foregoing reasons, Appellant submits that Claims 1-23 are non-obvious over the prior art. Appellant urges allowance of Claims 1-23.

Respectfully submitted,



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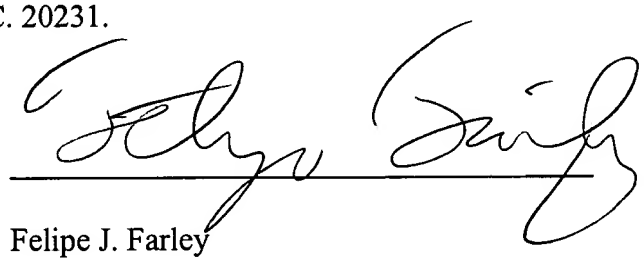
**CERTIFICATE OF MAILING UNDER 37 C.F.R. §1.8(a)**

I hereby certify that this Reply Brief, together with any paper referred to as being attached or enclosed, is being deposited with the United States Postal Service on the date shown below with sufficient postage as first-class mail in an envelope addressed to the Commissioner for Patents, Washington, D.C. 20231.



Felipe J. Farley

Date: December 4, 2000

## APPENDIX: CLAIMS ON APPEAL

1. A method for inducing an immune response against transformed, infected or diseased tissue comprising

removing only components present in the blood having a molecular weight of 120,000 daltons or less, until the transformed, infected, or diseased tissue is reduced in amount.

2. The method of claim 1 wherein the tissue is a solid tumor.

3. The method of claim 1 wherein the components are removed from one blood volume.

4. The method of claim 1 wherein the components are removed in multiple treatments.

5. The method of claim 1 further comprising treating the tissue with an agent selected from the group consisting of anti-angiogenic compounds, procoagulant compounds, cytokines, chemotherapeutic agents, and radiation.

6. The method of claim 5 wherein the agent is a cytokine and the cytokine is selected from the group consisting of GM-CSF, erythropoietin, thrombopoetin, G-CSF, M-CSF and SCF.

7. The method of claim 1 further comprising selectively removing soluble TNF receptor 1 and receptor 2 molecules.

8. The method of claim 1 further comprising vaccinating the patient with a vaccine against the transformed, infected or diseased tissue, wherein the vaccine is produced by immunization with antigens unique to the transformed, infected or diseased tissue.

9. A system for inducing an immune response against transformed, infected or diseased tissue comprising

a device for removing only components present in the blood having a molecular weight of 120,000 daltons or less, having inlet and outlet means for connection to a pump and tubing to recirculate the blood of a patient through the device.

10. The kit of claim 17 wherein the agent is an anti-angiogenic compound.

11. The kit of claim 17 wherein the agent is a procoagulant compound.

12. The kit of claim 17 wherein the agent is a cytokine.

13. The kit of claim 12 wherein the agent is a cytokine and the cytokine is selected from the group consisting of GM-CSF, erythropoietin, thrombopoetin, G-CSF, M-CSF and SCF.

14. The kit of claim 17 wherein the agent is a chemotherapeutic agent.

15. The kit of claim 14 wherein the agent is selected from the group consisting of alkylating agents, doxyrubicin, carboplatinum, cisplatinum, and taxol.

16. The system of claim 9 wherein the system includes means for administering radiation to the tissue.

17. A kit for treatment of a patient to induce an immune response against transformed, infected or diseased tissue comprising:

(a) a device for removing only components present in the blood having a molecular weight of 120,000 daltons or less, and

(b) an agent selected from the group consisting of anti-angiogenic compounds, procoagulant compounds, cytokines, chemotherapeutic agents, and radiation, in a dosage formulation for treatment of the patient in combination with treatment of the

patient with the device to remove blood components having a molecular weight of 120,000 daltons or less.

18. The system of claim 9 wherein the device is a capillary membrane filter with a pore size of between about 0.02 and 0.05 microns.

19. The system of claim 9 wherein the device is a parallel plate filter with a pore size of between about 0.04 and 0.08 microns.

20. The system of claim 9 wherein the device comprises filters with different pore sizes or geometries to provide for staggered removal of materials from the blood.

21. The system of claim 9 wherein the device is an absorbant column selectively removing specific cytokine or cellular inhibitors from the blood.

22. The system of claim 9 wherein the blood is plasma.

23. The kit of claim 17 further comprising anticoagulant to treat the device for removal of components from the blood prior to use.